

SEQUENCE LISTING

<110> Neta Ilan
Israel Vlodavsky
Oron Yacoby-Zeevi
Iris Pecker

<120> THERAPEUTIC AND COSMETIC USES OF HEPARANASES

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<170> PatentIn version 3.1

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Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
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Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
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Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
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Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
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Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu
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 Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg
 260 265 270
 Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu
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 Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr
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 Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile
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 385 390 395 400
 Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr
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 Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg
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 Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly
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 Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu
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 Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu
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| tcg cag tta gga gaa gat tat att caa ttg cat aaa ctt cta aga aag Ser Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys 240 245 250 255 | | | 827 |
| tcc acc ttc aaa aat gca aaa ctc tat ggt cct gat gtt ggt cag cct Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro 260 265 270 | | | 875 |
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<213> Homo sapiens

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| agagctctcg | actctccgct | gcgcggcgagc | tggcgggggg | agcagccagg | tgagcccaag | | 240 | |
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| Ser Ala Gly Gly Ser Ala Arg Ala Leu Asp Ser Pro Leu Arg Gly Ser | |
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| Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro Ala Gln Ala Gln Asp Val | |
| 75 80 85 | |
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| 90 95 100 | |
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| 105 110 115 | |
| ttc ctc atc ctc ctg ggt tct cca aag ctt cgt acc ttg gcc aga ggc | 498 |
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| ttg tct cct gcg tac ctg agg ttt ggt ggc acc aag aca gac ttc cta | 546 |
| Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu | |
| 140 145 150 | |
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| 155 160 165 | |
| caa tct caa gtc aac cag gat att tgc aaa tat gga tcc atc cct cct | 642 |
| Gln Ser Gln Val Asn Gln Asp Ile Cys Lys Tyr Gly Ser Ile Pro Pro | |
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| gat gtg gag gag aag tta cgg ttg gaa tgg ccc tac cag gag caa ttg | 690 |
| Asp Val Glu Glu Lys Leu Arg Leu Glu Trp Pro Tyr Gln Glu Gln Leu | |
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| cta ctc cga gaa cac tac cag aaa aag ttc aag aac agc acc tac tca | 738 |
| Leu Leu Arg Glu His Tyr Gln Lys Lys Phe Lys Asn Ser Thr Tyr Ser | |
| 200 205 210 215 | |
| aga agc tct gta gat gtg cta tac act ttt gca aac tgc tca gga ctg | 786 |
| Arg Ser Ser Val Asp Val Leu Tyr Thr Phe Ala Asn Cys Ser Gly Leu | |
| 220 225 230 | |
| gac ttg atc ttt ggc cta aat gcg tta tta aga aca gca gat ttg cag | 834 |
| Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Ala Asp Leu Gln | |
| 235 240 245 | |
| tgg aac agt tct aat gct cag ttg ctc ctg gac tac tgc tct tcc aag | 882 |
| Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys | |
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| ggg tat aac att tct tgg gaa cta ggc aat gaa cct aac agt ttc ctt | 930 |
| Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu | |
| 265 270 275 | |
| aag aag gct gat att ttc atc aat ggg tgc cag tta gga gaa gat tat | 978 |
| Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser Gln Leu Gly Glu Asp Tyr | |
| 280 285 290 295 | |

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| ctc tat ggt cct gat gtt ggt cag cct cga aga aag acg gct aag atg Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg Arg Lys Thr Ala Lys Met 315 320 325 | 1074 |
| ctg aag agc ttc ctg aag gct ggt gga gaa gtg att gat tca gtt aca Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Val Thr 330 335 340 | 1122 |
| tgg cat cac tac tat ttg aat gga cgg act gct acc agg gaa gat ttt Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg Glu Asp Phe 345 350 355 | 1170 |
| cta aac cct gat gta ttg gac att ttt att tca tct gtg caa aaa gtt Leu Asn Pro Asp Val Leu Asp Ile Phe Ile Ser Ser Val Gln Lys Val 360 365 370 375 | 1218 |
| ttc cag gtg gtt gag agc acc agg cct ggc aag aag gtc tgg tta gga Phe Gln Val Val Glu Ser Thr Arg Pro Gly Lys Lys Val Trp Leu Gly 380 385 390 | 1266 |
| gaa aca agc tct gca tat gga ggc gga gcg ccc ttg cta tcc gac acc Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asp Thr 395 400 405 | 1314 |
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| atg gga ata gaa gtg gtg atg agg caa gta ttc ttt gga gca gga aac Met Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn 425 430 435 | 1410 |
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| gga agt tca ctg ggc ttg cca gct ttc tca tat agt ttt ttt gtg ata Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser Tyr Ser Phe Phe Val Ile 570 575 580 | 1842 |
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Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser
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Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
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Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser
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Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val
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Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu
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Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser
145 150 155 160

Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu
165 170 175

Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn
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Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr

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| Asn | Ile | Ser | Trp | Glu | Leu | Gly | Asn | Glu | Pro | Asn | Ser | Phe | Trp | Lys | Lys |
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| Leu | His | Lys | Leu | Leu | Gln | Arg | Ser | Ala | Phe | Gln | Asn | Ala | Lys | Leu | Tyr |
| | | | 245 | | | | | | 250 | | | | | 255 | |
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| | | | 260 | | | | | 265 | | | | | 270 | | |
| Ser | Phe | Leu | Lys | Ala | Gly | Gly | Glu | Val | Ile | Asp | Ser | Leu | Thr | Trp | His |
| | | 275 | | | | | 280 | | | | | 285 | | | |
| His | Tyr | Tyr | Leu | Asn | Gly | Arg | Ile | Ala | Thr | Lys | Glu | Asp | Phe | Leu | Ser |
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| Ser | Asp | Ala | Leu | Asp | Thr | Phe | Ile | Leu | Ser | Val | Gln | Lys | Ile | Leu | Lys |
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| Val | Thr | Lys | Glu | Ile | Thr | Pro | Gly | Lys | Lys | Val | Trp | Leu | Gly | Glu | Thr |
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| Ser | Ser | Ala | Tyr | Gly | Gly | Gly | Ala | Pro | Leu | Leu | Ser | Asn | Thr | Phe | Ala |
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| Ala | Gly | Phe | Met | Trp | Leu | Asp | Lys | Leu | Gly | Leu | Ser | Ala | Gln | Met | Gly |
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| Ile | Glu | Val | Val | Met | Arg | Gln | Val | Phe | Phe | Gly | Ala | Gly | Asn | Tyr | His |
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| Leu | Phe | Lys | Lys | Leu | Val | Gly | Pro | Arg | Val | Leu | Leu | Ser | Arg | Val | Lys |
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| Gly | Pro | Asp | Arg | Ser | Lys | Leu | Arg | Val | Tyr | Leu | His | Cys | Thr | Asn | Val |
| | | | 420 | | | | | 425 | | | | | 430 | | |
| Tyr | His | Pro | Arg | Tyr | Gln | Glu | Gly | Asp | Leu | Thr | Leu | Tyr | Val | Leu | Asn |
| | | 435 | | | | | 440 | | | | | 445 | | | |
| Leu | His | Asn | Val | Thr | Lys | His | Leu | Lys | Val | Pro | Pro | Pro | Leu | Phe | Arg |
| | | 450 | | | | 455 | | | | | 460 | | | | |
| Lys | Pro | Val | Asp | Thr | Tyr | Leu | Leu | Lys | Pro | Ser | Gly | Pro | Asp | Gly | Leu |
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| Leu | Ser | Lys | Ser | Val | Gln | Leu | Asn | Gly | Gln | Ile | Leu | Lys | Met | Val | Asp |
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| Glu | Gln | Thr | Leu | Pro | Ala | Leu | Thr | Glu | Lys | Pro | Leu | Pro | Ala | Gly | Ser |
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| gtc aac cat gat att tgc agg tct gag ccg gtc tct gct gcg gtg ttg | 980 |
| Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val Leu | |
| 115 120 125 | |
| agg aaa ctc cag gtg gaa tgg ccc ttc cag gag ctg ttg ctg ctc cga | 1028 |
| Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu Arg | |
| 130 135 140 145 | |
| gag cag tac caa aag gag ttc aag aac agc acc tac tca aga agc tca | 1076 |
| Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser | |
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| Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu Ile | |
| 165 170 175 | |
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| Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn Ser | |
| 180 185 190 | |
| tcc aac gcc cag ctt ctc ctt gac tac tgc tct tcc aag ggt tat aac | 1220 |
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| Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys Ala | |
| 210 215 220 225 | |
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| His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu Leu | |
| 230 235 240 | |
| cat aaa ctt cta caa agg tca gct ttc caa aat gca aaa ctc tat ggt | 1364 |
| His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr Gly | |
| 245 250 255 | |
| cct gac atc ggt cag cct cga ggg aag aca gtt aaa ctg ctg agg agt | 1412 |
| Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg Ser | |
| 260 265 270 | |
| ttc ctg aag gct ggc gga gaa gtg atc gac tct ctt aca tgg cat cac | 1460 |
| Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His His | |
| 275 280 285 | |
| tat tac ttg aat gga cgc atc gct acc aaa gaa gat ttt ctg agc tct | 1508 |
| Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser Ser | |
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| gat gcg ctg gac act ttt att ctc tct gtg caa aaa att ctg aag gtc | 1556 |
| Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys Val | |
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| Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser | |
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| Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly Ile | |
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| gaa gtc gtg atg agg cag gtg ttc ttc gga gca ggc aac tac cac tta | 1748 |
| Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu | |
| 370 375 380 385 | |
| gtg gat gaa aac ttt gag cct tta cct gat tac tgg ctc tct ctt ctg | 1796 |
| Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu | |
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| | |
|--|------|
| Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys Gly | |
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| Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val Tyr | |
| 420 425 430 | |
| cac cca cga tat cag gaa gga gat cta act ctg tat gtc ctg aac ctc | 1940 |
| His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn Leu | |
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| His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg Lys | |
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| Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu Leu | |
| 470 475 480 | |
| tcc aaa tct gtc caa ctg aac ggt caa att ctg aag atg gtg gat gag | 2084 |
| Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp Glu | |
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| cag acc ctg cca gct ttg aca gaa aaa cct ctc ccc gca gga agt gca | 2132 |
| Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser Ala | |
| 500 505 510 | |
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| Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn Ala | |
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| Lys Ile Ala Ala Cys Ile | |
| 530 535 | |
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| cggttcctca ccttcctgag ctctccacgg cttcgagccc tgtctagagg cttatctcct | 240 |
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| cattaactgt caccacctgc agtgggtctac ttagagaaca ccgcactgga tgtaaacact | 180 |
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